THE LANCET
Respiratory Medicine

Supplementary appendix 2

Appendix Methods

High-resolution Computed Tomography (HRCT) scans and image analysis

Patients underwent chest non-contrast enhanced CT examinations in the supine position and with breath-holding following inspiration (GE Healthcare Optima CT680). The technical parameters included a 64-section scanner with 1 mm collimation at 5 mm intervals. Images were obtained with both mediastinal (width 350 HU; level 50 HU) and parenchymal (width 1500 HU; level -700 HU) window settings. The follow-up patients completed HRCT scan testing every 3 months.

For imaging evaluations, 2 radiologists, with 5 and 27 years of thoracic radiology experience, respectively, reviewed the images independently, with a final finding reached by consensus when there was a discrepancy. They were blinded to the clinical information or clinical progress of the patients, except for the knowledge that these were cases of COVID-19 patients.

The pneumonia CT scores of patients during hospitalisation were recorded with a method described previously[1]. In brief, the CT features in hospitalised COVID-19 patients included ground glass opacity (GGO), consolidation, air bronchogram, nodular opacities and pleural effusion. The CT scans were scored on the axial images. The extent of involvement of each abnormality was assessed independently for each of 3 zones: upper (above the carina), middle (below the carina and above the inferior pulmonary vein), and lower (below the inferior pulmonary vein). The CT findings were graded on a 3-point scale: normal attenuation (1), GGO (2), and consolidation (3). Each

lung zone, with a total of 6 lung zones in each patient, was assigned a following scale according to distribution of the affected lung parenchyma: normal (0), <25% abnormality (1), 25–50% abnormality (2), 50–75% abnormality (3), and >75% abnormality (4). The 4-point scale of the lung parenchyma distribution was then multiplied by the radiologic scale described above. Points from all zones were added for a final total cumulative score (HRCT pneumonia score during hospitalisation), with value ranging from 0 to 72. The peak pneumonia CT score is the highest pneumonia CT score for a patient during COVID-related hospitalisation.

To analyse follow-up HRCT scans, HRCT findings were initially evaluated based on key features[2] and then scored based on a method adapted from Ichikado and colleagues[3], here named HRCT follow-up score, which allowed us to evaluate interstitial changes in lungs[3]. Briefly, the lungs were divided into 6 zones (upper, middle, and lower on both sides), each zone was evaluated separately and for each zone the CT findings were graded on a 6-point scale: areas with (1) normal attenuation, (2) GGO without traction bronchiectasis or bronchiolectasis, (3) consolidation without traction bronchiectasis or bronchiolectasis, (4) GGO with traction bronchiectasis or bronchiolectasis, (5) consolidation with traction bronchiectasis or bronchiolectasis, and (6) honeycombing. The upper lung zone was defined as the area of the lung above the level of the tracheal carina, the lower lung zone was defined as the area of the lung below the level of the inferior pulmonary vein, and the middle lung zone was defined as the area of the lung between the upper and lower zones. Abnormal findings and the

43   extent of lung involvement was evaluated visually and independently for each of the 6

44   zones. The scores were based on the percentage of the lung parenchyma that showed

45   evidence of the abnormality and were estimated to the nearest 5 % of parenchymal

46   involvement. Scores from all zones were added for a final total cumulative score, with

47   value ranging from 6 to 36.

References:

1. Liu X, Zhou H, Zhou Y, et al. Temporal radiographic changes in COVID-19 patients: relationship to disease severity and viral clearance. *Scientific Reports* 2020; **10**(1): 10263.

2. Hansell DM, Bankier AA, MacMahon H, McLoud TC, Muller NL, Remy J. Fleischner Society: glossary of terms for thoracic imaging. *Radiology* 2008; **246**(3): 697-722.

3. Ichikado K, Suga M, Muller NL, et al. Acute interstitial pneumonia: comparison of high-resolution computed tomography findings between survivors and nonsurvivors. *American journal of respiratory and critical care medicine* 2002; **165**(11): 1551-6.

59 **Appendix Figures**

60 **Appendix Figure S1.** Impact of severe COVID-19 on follow-up 6-minute walking
61 distance (6MWD) test. Graph showing temporal changes in 6MWD at 3, 6, 9 and 12
62 months after discharge. Median, IQR (interquartile range) and P values are indicated.
63 Values are % of predicted.

64
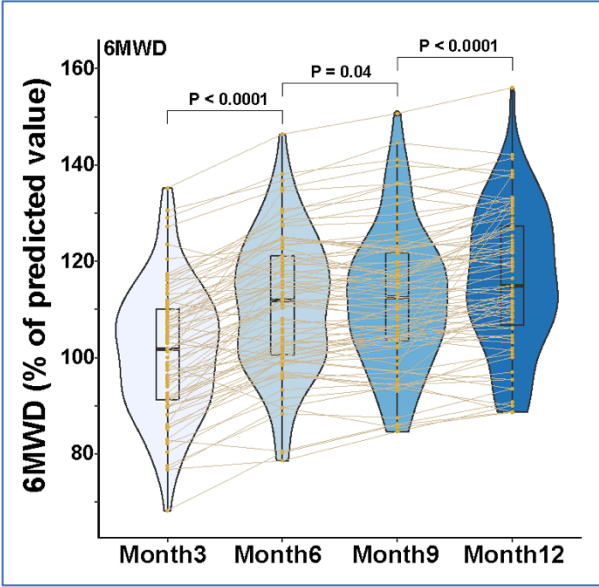
65 **Appendix Figure S2.** Radiographic features of HRCT scans following severe COVID-
66 19 related hospitalisation. Representative HRCT images showing (**A**) ground-glass
67 opacity; (**B**) interlobular septal thickening; (**C**) reticular opacity; (**D**) subpleural
68 curvilinear opacity; (**E**) mosaic attenuation; and (**F**) bronchiectasis, highlighted with
69 red arrows.
70
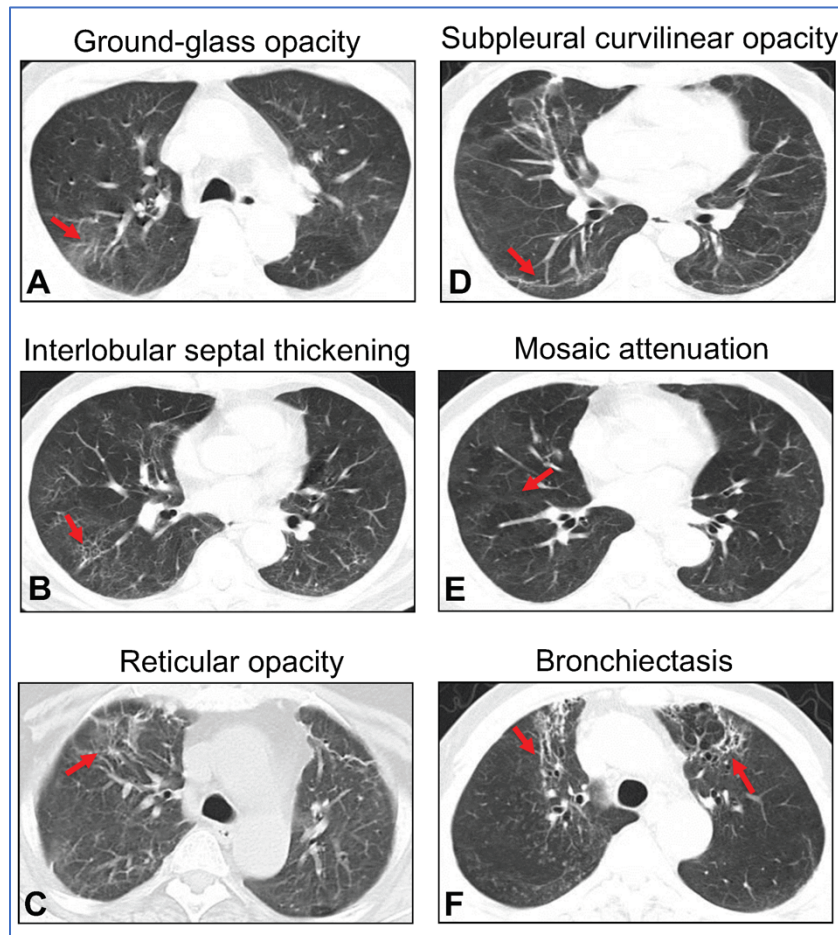
Appendix Figure S3. Temporal changes in HRCT scans following severe COVID-19 related hospitalisation. Representative temporal radiographic changes in a 50 male patient with severe COVID-19 with all radiographic changes resolving by 6 months in (**A**); whilst in (**B**) a 54 male patient with severe COVID-19 where radiographic changes persist at 12 months. (**C**) Graph showing temporal HRCT Follow-up score changes in patients with normal (score = 6, blue) or abnormal (score ≥ 7, red) HRCT scans at 12 months after discharge. P values are indicated. (**D**) Graph showing peak HRCT Pneumonia score during hospitalisation in patients with normal *vs.* abnormal HRCT scans at 12 months after discharge. Data are median and IQR (interquartile range) with P values indicated.
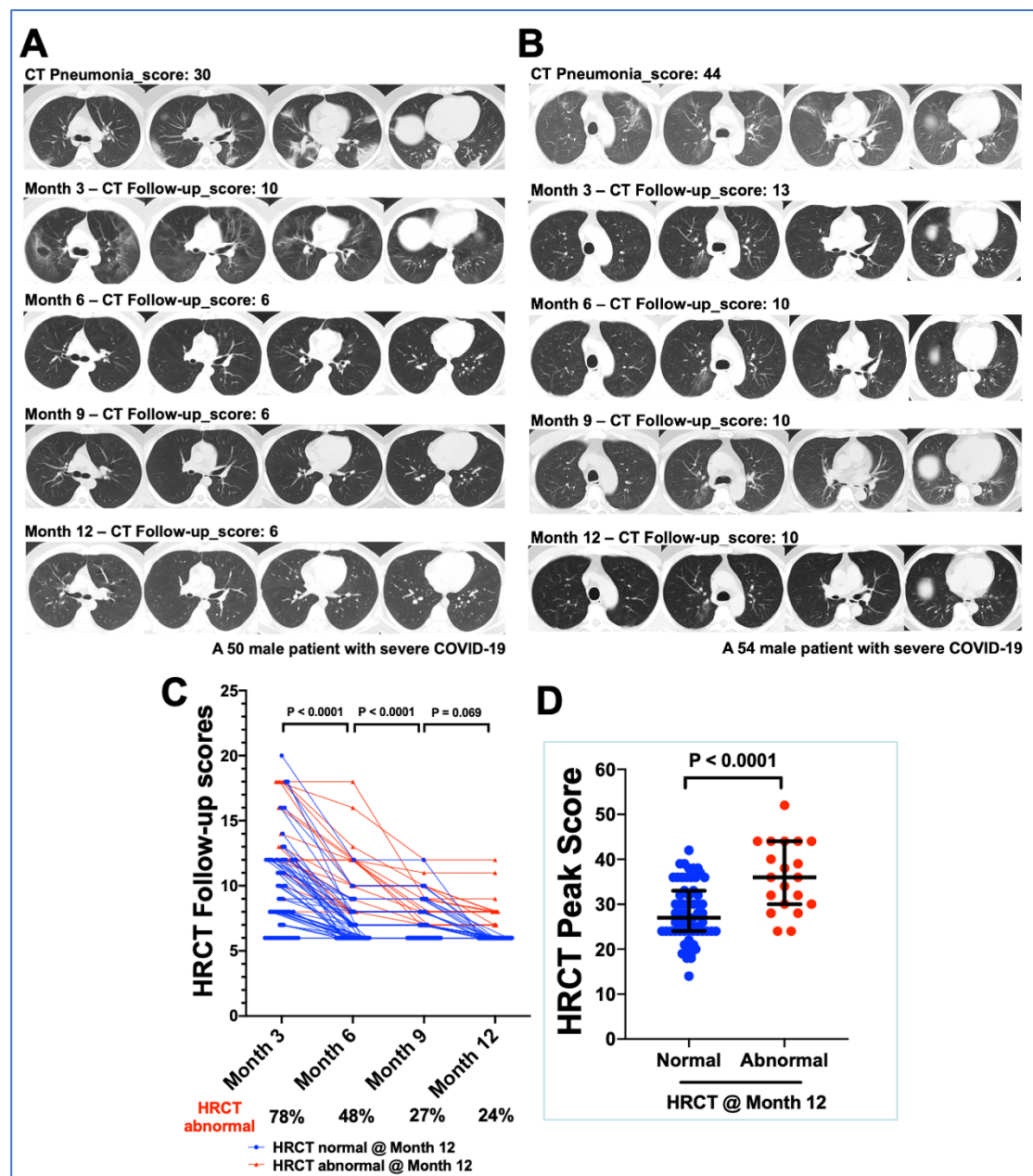
Appendix Tables

Appendix Table S1. Results of serial pulmonary function tests among recovered severe COVID-19 patients who did not require mechanical ventilation (N = 83).

Parameter	@ Month 3	@ Month 6	@ Month 12	P value[a]	P value[b]
DLCO (% of predicted)	77 (67 ~ 87)	76 (68 ~ 90)	88 (78 ~ 101)	0.691	*< 0.0001*
FEF25-75% (% of predicted)	91 (64 ~ 109)	89 (67 ~ 103)	89 (76 ~ 111)	1	*0.032*
FEV1/FVC (% of predicted)	81 (77 ~ 84)	81 (78 ~ 84)	82 (79 ~ 86)	1	0.099
FRC (% of predicted)	89 (78 ~ 104)	89 (81 ~ 106)	102 (87 ~ 118)	1	*< 0.0001*
FVC (% of predicted)	92 (81 ~ 99)	94 (85 ~ 104)	98 (89 ~ 109)	*0.002*	*< 0.0001*
FEV1 (% of predicted)	90 (76 ~ 100)	92 (80 ~ 101)	96 (85 ~ 110)	0.206	*< 0.0001*
RV (% of predicted)	81 (69 ~ 97)	81 (72 ~ 100)	85 (72 ~ 99)	0.963	1
TLC (% of predicted)	87 (77 ~ 98)	91 (82 ~ 98)	92 (87 ~ 100)	*0.004*	*< 0.0001*
VC (% of predicted)	91 (81 ~ 103)	95 (83 ~ 104)	98 (90 ~ 111)	*0.006*	*< 0.0001*

DLCO, diffusing capacity of the lungs for carbon monoxide; $FEF_{25-75\%}$, forced expiratory flow between 25% and 75% of FVC; FRC, functional residual capacity; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; RV, residual volume; TLC, total lung capacity; VC, vital capacity. Values are expressed as median (interquartile range). [a]Month 6 *vs.* 3. [b]Month 12 *vs.* 6.

90 **Appendix Table S2.** Frequency of pulmonary function parameters below normal range
91 in recovered severe COVID-19 patients who did not require mechanical ventilation (N
92 = 83).
93

	< 60% predicted value			< 80% predicted value		
	@ Month 3	@ Month 6	@ Month 12	@ Month 3	@ Month 6	@ Month 12
DLCO	12 (15%)	11 (13%)	4 (5%)	46 (55%)	45 (54%)	27 (33%)
FRC	6 (7%)	6 (7%)	2 (2%)	23 (28%)	18 (22%)	10 (12%)
FVC	4 (5%)	2 (2%)	0 (0%)	19 (23%)	13 (16%)	9 (11%)
FEV1	6 (7%)	4 (5%)	3 (4%)	25 (30%)	20 (24%)	13 (16%)
RV	12 (15%)	9 (11%)	11 (13%)	38 (46%)	35 (42%)	32 (39%)
TLC	9 (11%)	4 (5%)	3 (4%)	22 (27%)	16 (19%)	12 (15%)
VC	4 (5%)	2 (2%)	1 (1%)	20 (24%)	15 (18%)	9 (11%)

94 DLCO, diffusing capacity of the lungs for carbon monoxide; FRC, functional residual capacity; FVC, forced vital
95 capacity; FEV1, forced expiratory volume in 1 second; RV, residual volume; TLC, total lung capacity; VC, vital
96 capacity. Values are N (%).

97 **Appendix Table S3.** Univariate and multivariate logistic regression analysis in severe
98 COVID-19 patients who did not require mechanical ventilation for risk factors
99 associated with diffusion deficit at 12 months after discharge (N = 83).
100

	OR (odds ratio)	95% CI (confidence interval)	P - value
Univariate			
Age	1.03	0.99 ~ 1.08	0.140
Gender (Female)	7.14	2.53 ~ 20.16	***0.0002***
BMI	0.94	0.80 ~ 1.10	0.429
Length of hospital stay	1.00	0.93 ~ 1.07	0.952
Peak CT Pneumonia_score during hospitalization	1.00	0.94 ~ 1.06	0.876
HFNC/NIV	1.58	0.62 ~ 4.06	0.339
Oseltamivir	0.75	0.29 ~ 1.92	0.546
Ganciclovir	1.34	0.53 ~ 3.38	0.531
Multivariate			
Age	1.06	1.00 ~ 1.12	0.063
Gender (Female)	8.61	2.83 ~ 26.2	***0.0002***
Peak CT Pneumonia_score during hospitalization	0.98	0.91 ~ 1.05	0.521

101 BMI, body mass index; HFNC, high-flow nasal cannula; NIV, non-invasive mechanical ventilation.

102   **Appendix Table S4.** HRCT features among recovered severe COVID-19 patients who
103   did not require mechanical ventilation (N = 83).
104

	@ Month 3	@ Month 6	@ Month 9	@ Month 12	P value[a]	P value[b]	P value[c]
Ground-glass opacity	65 (78%)	38 (46%)	20 (24%)	19 (23%)	***< 0.0001***	***0.010***	1
Interlobular septal thickening	28 (34%)	11 (13%)	4 (5%)	4 (5%)	***0.006***	0.174	1
Reticular opacity	27 (33%)	13 (16%)	3 (4%)	3 (4%)	***0.033***	***0.026***	1
Subpleural curvilinear opacity	9 (11%)	4 (5%)	1 (1%)	1 (1%)	0.446	1	1
Mosaic attenuation	2 (2%)	3 (4%)	3 (4%)	3 (4%)	1	1	1
Bronchiectasis	1 (1%)	1 (1%)	1 (1%)	1 (1%)	1	1	1

105   [a]Month 6 *vs.* 3. [b]Month 9 *vs.*6. [c]Month 12 *vs.*9. Values are N (%).

106   **Appendix Table S5.** Univariate and multivariate logistic regression analysis in severe
107   COVID-19 patients who did not require mechanical ventilation for risk factors
108   associated with abnormal HRCT at 12 months after discharge (N = 83).
109

	OR (odds ratio)	95% CI (confidence interval)	P - value
Univariate			
Age	1.02	0.97 ~ 1.07	0.401
Gender	1.86	0.67 ~ 5.13	0.232
BMI	0.92	0.77 ~ 1.10	0.357
Length of hospital stay	1.09	1.01 ~ 1.19	***0.031***
Peak CT Pneumonia_score during hospitalization	1.18	1.08 ~ 1.29	***0.0002***
HFNC/NIV	3.10	1.00 ~ 9.55	***0.049***
Oseltamivir	1.97	0.64 ~ 6.12	0.239
Ganciclovir	1.65	0.59 ~ 4.59	0.337
Multivariate			
Peak CT Pneumonia_score during hospitalization	1.36	1.13 ~ 1.62	***0.0009***
Length of hospital stay	0.92	0.81 ~ 1.04	0.180
HFNC/NIV	0.24	0.04 ~ 1.63	0.146

110   BMI, body mass index. HFNC, high-flow nasal cannula; NIV, non-invasive mechanical ventilation.